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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HAQ, SHAFIQUL	

ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
03/12/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/533,950	ROGET ET AL.	
	Examiner	Art Unit	
	SHAFIQUL HAQ	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 10-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 10-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/22/2008 has been entered.

Status of claims

2. Applicant's amendments and arguments filed 12/28/07 is acknowledged and entered. Claims 1-6 and 10-25 are pending and are examined on merits.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-3, 6, 10-21 and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Livache et al (Biosensors and Bioelectronics 1998) in view of Guedon *et al* (Anal Chem. 2000).

Livache *et al* disclose a method of immobilization of biological material (e.g. peptides, protein. See the Title) (lines 14-15, right column of page 629) to a conductive support (e.g biochip) by means of a pyrrole polymer (see abstract and introduction). The method comprises coupling peptides to dT10 activated pyrrole

monomer (i.e. to activated pyrrole monomer) (see section 2.1. of page 630) to provide peptide pyrrole coupling compound and mixing solutions of pyrrole monomer (which is not coupled to peptide) and the peptide-pyrrole to obtain an electropolymerization solution and elctropolymerization to obtain a film of copolymer on conductive medium (see sections 2.1. and 2.3. of page 630). The pyrrole copolymerization process allows the preparation of addressed probes such as polypyrrole-DNA or equivalent polypyrrole-protein on blocks of biosensor array (see section 3.; fig.5 and lines 6-9, right column of page 633) for detection of DNA or other equivalent analyte such as proteins. Examples of immobilization of proteins (e.g. ACTH hormone) and DNA (Fig. 5; Fig.6 and section 3.4.) are also disclosed.

Livache et al disclose different thickness (from 2 to 80 nm approximately) which were obtained by applying an amount of current from 10 to 400uC/mm^2 (section 3.2., 3.4. and Fig. 4) but do not mention electopolymerization being carried out with a charge of less that 50uC/mm^2, for a synthesis time of less than 1000ms.

Guedon *et al* in a polypyrrole-based DNA sensor disclose six different thicknesses of polypyrroly-ODN spots made by performing the synthesis for 250ms to 1000ms leading to 9-14 nm thick films (page 6007, left column, left column, lines 3-12). The film synthesis is very fast taking about 500ms to spot an 11 nm thick film by a 2-V electrochemical pulse (page 6004, lines 30-31 of left column and page 6005, left column, lines 7-8). Goedon *et al* also disclose that for optimal hybridization signal, optimal thickness of the spot was found to be close to 11 nm (see abstract; page 6007, lines 1-1-26 of left column and Fig. 6).

Therefore, given the above fact that a film of pyrrole containing copolymer having a thickness close to 11 nm is desirable for optimal hybridization signal (Guedon et al) in a pyrrole based DNA sensor, it would have been prima facie obvious to one of ordinary skill in the art at the time of the instant invention to provide similar polymer film thickness close to 11nm (i.e 10nm) in the pyrrole based biosensor of Livache et al, with the expectation of enhancing detection signal with a reasonable expectation of success and to produce a thickness close to nm within 250ms to 1000ms (Goedon) with a electrode of 50um x 50um, an electric current of less that 50uC/mm^2 would be obvious as described above. Optimal thickness of 11 mm is disclosed by Guedon *et al* for DNA based sensor but, however, the optimal thickness for a particular application for other biosensors (such as pyrrole based protein sensor as disclosed by Livache) can be obtain by routine optimization, which can be produced by varying electric current and synthesis time as taught by Guedon *et al* . Protein is considered as an equivalent analyte to DNA by Livache *et al* (se the title for "DNA or peptide array" and section 2.3. wherein "OND or peptide" is recited) and thus one of ordinary skill in the art would also first consider starting with the thickness as described by Guedon *et al* for similarly optimizing the pyrrole-protein thickness of the protein based sensor of Leviche for optimal detection sensitivity.

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the .general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233,235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed

from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 .("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.)

With regard to claim 2, Levache *et al* teach that the pyrrole copolymerization process allows the preparation of addressed polypyrrole-DNA/protein on blocks of biosensor array (see section 3.; fig.5 and lines 6-9, right column of page 633) and with regard to claim 3, Livache *et al* teach activating pyrrole through dT10 oligonucleotide linker and coupling to peptides (see section 2.1.).

With regard to claims 10-14, Livache *et al* teach immobilization of biological materials (e.g. peptides, protein) (lines 14-15, right column of page 629) to conductive support to provide biosensors and immobilization of different variation of binding partners on the sensor surface with the expectation of analysis of different analytes would be obvious to one of ordinary skill in the art and one of ordinary skill in the art would expect such substitution of one binding partner with another to result in an equivalently useful biosensor for analysis of different analytes.

With regard to the polymer film thickness of claims 15-16 and 23-25, as described above, the optimal thickness for a particular application can be obtain by routine optimization, which can be produced by varying electric current and synthesis time as taught by Guedon *et al*.

As for location of the conductive support to biosensor device and use of the biosensor device for different purposes (claims 17-21), Livache's conductive support is meant to be used as biosensors and the location and use of the conductive support constitute obvious variations in parameters which are routinely modified in the art and which have not been described as critical to the practice of the invention.

5. Claims 4, 5 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Livache et al (Biosensors and Bioelectronics 1998) in view of Guedon et al (Anal Chem. 2000) as described above, and further in view of either of Domb *et al* (US 2006/0013850 A1) or Caillat et al (US 6,803,228).

Livache et al in view of Guedon *et al* disclose a method of immobilization of proteins to a conductive support (e.g biochip) by means of a pyrrole polymer as describes above, but the references fail to disclose pyrrole functionalized with succinimide or maleimide for coupling to protein and ODN.

Domb (US 2006/0013850 A1) discloses coating of electropolymerized pyrrole polymers to conductive support (paragraphs [0019], [0027]). Domb also discloses that the electropolymerized polymer can have a second monomer bearing a reactive group/ functional group (paragraphs [0032], [0044], [0051] and [0055]) for binding to bioactive agents such as proteins, enzymes, nucleic acids (paragraph [0024], [0182], [0243], [0244]). Domb further discloses that activated pyrrole monomers {(e.g. N-alkyl pyrrole derivatives possessing functional groups such as carboxylic acid and derivatives thereof (e.g. acyl halide, ester), amine, hydroxyl, vinyl, acetylene and thiol} can be used for binding bioactive agents (paragraphs [0209], [0396] and

example 1, especially scheme 1, scheme 2). Domb *et al* further teach activation of pyrrole with activating agent N-hydroxysuccinimide (see paragraph [0292] for PPA-NHS). Domb et al. further discloses conditions for attachment of bioactive agent such as peptides and proteins to activated pyrrole monomers (paragraph [0396] and [0397]).

Caillat *et al* also disclose pyrrole polymer functionalized with N-hydroxysuccinimide and maleimide for coupling to biomolecules (see 3rd compound from top in column 4 and lines 63-67). Caillat *et al* further teach use of bifunctional crosslinking agent (e.g. comprising N-hydroxysuccinimide ester function and a maleimide function) (column 4, lines 63-67) for activation of pyrrole.

Therefore, given the fact that functionalization of pyrrole with N-hydroxysuccinimide or maleimide is know and common in the art (Domb and Caillat *et al*) for activation of pyrrole for coupling to biomolecules, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to also activate the pyrrole monomer of Livache *et al* with other commonly used activation groups such as succinimide or maleimide with the expectation of similarly producing activated pyrrole useful for producing conductive support containg polymer of pyrrole coupled with protein with a reasonable expectation of success.

With regard to Claims 5 and 22, Domb *et al* and Caillat *et al* teach activation of pyrrole with activating agent such as succinimide and heterobifunctional reagent. Caillat *et al* teach heterobifunctional crosslinking agents comprising maleimido and NHS group and at least one of the heterobifunctioanal group such as GMBS when

linked to amine nitrogen of pyrrole or N-ethylamine pyrrole through NHS group of GMBS would provide a linker that would either read or would be obvious to the linkers of claims 5 and 22 absent unexpected results. Since the general conditions for providing activated pyrrole are disclosed in prior art and since as the activating groups that provides linkers of claims 5 and 22 do not seem to be critical to the practice of this invention, the use of commonly known activating group would be obvious to one of ordinary skill in the art for optimization absent unexpected results.

Response to Applicant's argument

6. Applicant's arguments filed 12/22/08 have been fully considered but are rendered moot in view of the new ground of rejection presented in this office action.

However, with regard to Domb, Applicants argued that the Domb priority document PCT '807 does not expressly describe the pyrrole-protein coupling compound, and mixing such a coupling compound with a second solution of uncoupled pyrrole monomer as required by present claims. Applicants further argued that lines 1-6 on page 19 refer to "direct esterification to aminopropyl pyrrole" of "hydroxyl containing bioactive molecules" using carbodiimide. Wlile peptides may contain hydroxyl side-chains, this section id silent with respect to production of protein-pyrrole coupling compound and mixing such a coupling compound with a second solution of uncoupled pyrrole monomer as required by ptesent claims.

Applicants' arguments have been fully considered but are not persuasive because PCT '807 clearly discloses activation of pyrrole with functional group for coupling with active agent through covalent linkages and the active agent can be a

protein such as an enzyme (line 15-16 and 21 on page 12). PCT '907 teach conjugation of an amino containing pyrrole derivative with an active agents having reactive group such as carboxylic acid (note that protein contains carboxylic acid group) using DCC as coupling agent (page 18, lines 1-9). Further, carbodiimide activation of carboxylic acid containing molecules for conjugation with an amine containing molecule is a well known reaction mechanism and one of ordinary skill in the art could easily rnvision activation of carboxylic acid containing molecule (e.g. activation of carboxylic acid containing pyrrole or activation of carboxylic acid containing protein) for conjugation to an amine containing protein or to amine containing pyrrole and vice versa. Moreover, page 18, lines 26-28 specifically teach conjugation of bioactive peptide or proteinic molecules via their carboxylic acid or lysyl residues to either aminopropyl pyrrole or to carboxyethyl pyrrole using the carbodiimide coupling procedure. Therefore, coupling of pyrrole to a protein in PCT '807 is not a new matter for Domb (US 2006/0013850).

Wit regard to optimal thickness, see the discussion in paragraph 4 of this office action.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHAFIQUL HAQ whose telephone number is (571)272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on 571-272-0806. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shafiqul Haq/
Examiner, Art Unit 1641